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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/434,382	11/05/99	TAVTIGIAN	S 2318-247

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EXAMINER	
HUNT, J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/434,382	Tavtigian et al.
Examiner	**Group Art Unit**
Jennifer Hunt	1642

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-60* is/are pending in the application.

Of the above, claim(s) *16-24 and 27-60* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-15, 25, and 26* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-15 and 25-26, in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-60 are pending in the application. Claims 16-24 and 27-60 have been withdrawn from consideration by the examiner, as they are drawn to a non-elected invention. Claims 1-15 and 25-26 are addressed herein.

Claim Objections

2. Claim 1 is objected to because it contains a typographical error: The term "comprising" in line 1 of the claim is misspelled. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

3. Claims 1-15 and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claims 1-15 and 25-26 are improper because they use the abbreviation HPC2, without identifying which HPC2 they refer to.

5. Claims 1-7 and 9-15 are unclear in the recitation of "a modified form which is functionally equivalent". The metes and bounds of the encompassed compositions cannot be determined. Specifically, it cannot be determined what would be considered "modified" and "functionally equivalent". For example, at what point of difference would a composition cease to be a "modified version", and instead be considered a completely different composition? Further, what is a functional equivalent? Must the compositions be identical in function, or are some variations permitted? And if so, what variations would be permitted and what variations would not?

6. Claims 2 and 8-9 are unclear in the recitation of stringent conditions. The metes and bounds of "stringent conditions" cannot be determined. It is not clear what conditions would be considered "stringent" and what would not. Although the claims need not recite the exact conditions, there must be some guidance or teaching which would permit one of skill in the art to definitively determine what would constitute "stringent conditions".

7. Claims 2, 4, and 6-9 are unclear in the recitation of "corresponding RNA". The metes and bounds of corresponding RNA cannot be determined. It is not possible to determine what RNA would be considered "corresponding" and what would not. For example, at what point of difference would an RNA cease to be "corresponding", and instead be considered a completely different RNA?

8. Claims 4, 9, and 26 are unclear in the recitation of "allelic variant". The metes and bounds of an allelic variant cannot be determined. Specifically it is not possible to ascertain what would be considered an allelic variant and what would not. For example, at what point of difference would a composition cease to be an "allelic variant", and instead be considered a completely different composition?

9. Claims 5-7, 9, and 26 are unclear in the recitation of "mutated form". The metes and bounds of mutated form cannot be determined. Specifically it is not possible to ascertain what would be considered a mutated form and what would not. For example, at what point of difference would a composition cease to be a "mutated form", and instead be considered a completely different composition?

10. Claim 10 is unclear in the recitation of "said nucleic acid" in line 3. It is not clear if "said nucleic acid" refers to the nucleic acid probes, or the nucleic acid of claim 1.

11. Claim 12 recites the limitation "the coding sequence for the HPC2 polypeptide" and "said coding sequence". There is insufficient antecedent basis for this limitation in the claim.

12. Claim 12 is unclear in the recitation of "capable of directing the expression". The metes and bounds of "capable of directing the expression" cannot be determined. It is not clear what would be considered "capable of directing the expression" and what would not. For example, would something which is "capable of" performing a function only under extreme or unusual conditions meet the limitation? If so, at what point would a composition no longer meet the limitation? And further, what is encompassed by "directing the expression"? Does any

composition which plays a role in expression level meet the limitation, or must the composition be the regulator which controls expression?

13. Claim 25 is unclear in the recitation of "derived from". The metes and bounds of derived from cannot be determined. Specifically it is not possible to ascertain what would be considered derived from and what would not. For example, at what point of difference would a composition cease to be "derived from", and instead be considered a completely different composition?

14. Claim 26 is unclear because it cannot be determined if "for determination of all or part of the sequence of the HPC2 gene" and "having the nucleotide sequence set forth in SEQ ID NO:1..." refer to the primers of claim 25, or of claim 26, and further it cannot be determined if "having the nucleotide sequence set forth in SEQ ID NO:1..." refers to the primers themselves, or "all or part of the sequence of the HPC2 gene". Further clarification of the claim language is required.

With regard to the rejections under 112 second paragraph detailed above, although the specification provides some limited guidance as to the meaning of modified variants, fragments, corresponding molecules, etc., the teachings in the specification fail to assert specific metes and bounds. Pointing to a place in the specification, or in the teachings of the prior art, which distinctly defines the rejected terminology would bring favorable consideration.

15. Claims 1-15 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection

Claims 1-15 and 25-26 are broadly drawn nucleic acids of any size, including mutants, modified forms, and variants thereof, which contain a part of SEQ ID NO: 1, or the nucleic acid sequence encoding SEQ ID NO:2. The claims are drawn to a polynucleotide of any size which is only defined by a small number of nucleic acid resides, hence the claims are drawn to nucleic acid sequences which minimally contain only portions of SEQ ID NO:1, or the nucleic acid sequence encoding SEQ ID NO:2. Thus the claims are drawn to a large genus of molecules. In the case of small identified nucleic acid sequences claimed with open language, the genus of the polynucleotides comprising a partial sequence encompasses a variety of subgenera with widely varying attributes. The specification discloses only the structural features of one species, the polynucleotide of SEQ ID NO:1 and the polypeptide of SEQ ID NO: 2, which is encoded by SEQ ID NO:1. Further, claim 25 as recited, reads on *any* pair of oligonucleotide primers, not limited to SEQ ID NO:1 primers, or even HPC2 primers, because intended use and method of making a product carry no weight with respect to patentability.

Thus the specification lacks information to lead one of ordinary skill in the art to understand that the applicant had possession of the broadly claimed genus of polynucleotides at

the time the instant application was filed. Applicant is referred to the interim guidelines 112, first paragraph, published in the Official gazette and also available on www.uspto.gov.

16. Claims 1-15 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability of the unpredictability of the art, and 8) the breadth of the claims (see Ex parte Forman, 230 USPQ 546, BPAI, 1986).

The claims are broadly drawn to polynucleotides of any size, provided that they share some sequence similarity with the polynucleotide encoding the HPC2 polypeptide of SEQ ID NO:2 or the polynucleotide of SEQ ID NO:1, and any mutants, variants, modifications, etc. thereof.

The specification teaches the polynucleotide of SEQ ID NO:1, derived from cDNA libraries screened for a Chromosome 17 mutation which correlates to an increased risk of prostate cancer. The specification teaches an open reading frame for the polypeptide, as well as the exonic and intronic sections, theoretical methods of expression, and production of antibodies

to portions of the polypeptide. There is a prophetic example of gene analysis (Example 8), but this example is merely an invitation/wish list for future experimentation and provides no information about the gene beyond what is summarized above.

Thus the claims are broadly drawn to literally almost any polynucleotide, provided that it has minimal correlation to the polynucleotide encoding SEQ ID NO:2 , or to SEQ ID NO:1. Further, it is well established in the art that predicting the how alterations, mutations, modifications of a polynucleotide will affect the encoded polypeptide is difficult and unpredictable, and well out of the realm of routine experimentation.

For example, Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence

are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. In addition, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3).

Further, the disclosure of one HPC2 polynucleotide which presumably encodes the corresponding polypeptide is insufficient support under the first paragraph of 35 U.S.C 112 for

claims which encompass any and all HPC2 polypeptides, mutants, variants, and modifications thereof, including fragments thereof and HPC2 polypeptides which are yet undiscovered. The courts have held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based In some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not In compliance with the first paragraph of U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill In the art; In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement In the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; In cases involving unpredictable factors, such as chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."In re Fisher 427 F.2d 833, 166 USPQ 18 (CCPA 1970)

Thus for the reasons set forth above, specifically, because of the large breadth of the claims, the limited guidance provided in the specification, the relative lack of predictability and skill of those in the art with regard to determining how alteration of nucleic acid sequences corresponds to protein structure and function, one of skill in the art would not be enabled to make the invention.

Claim Rejections - 35 U.S.C. § 102

17. Claims 2, 8, 9, are rejected under 35 U.S.C. 102(a) as being anticipated by Accession AC005277, IDS AN.

AC005277 comprises or "has" a polynucleotide of at least 15 nucleotides which hybridizes to the nucleic acid of claim 1, and has a nucleotide sequence encompassed by claim 8.

18. Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Ohagi et al., PNAS, Vol. 89, pages 4977-4981.

Ohagi et al. teaches a pair of single stranded oligonucleotide primers for determination of a nucleotide sequence of a HPC2 gene, said sequence being derived from genomic clones for HPC2, and the use of said primers resulting in a nucleic acid amplification reaction resulting in the synthesis of DNA or RNA corresponding to all or part of the sequence of the HPC2 gene.(see

materials and methods, pages 4977-8) Although the HPC2 gene of Ohagi et al. encodes a serine protease, and not a "cancer predicting gene", the instant teachings meet the limitation of the claim, which does not differentiate the HPC2, except by a laboratory designation, which is an arbitrary designation.

It is noted that claim 25, as recited, reads on *any* pair of oligonucleotide primers, as intended use and method of making a product carry no weight with respect to patentability.

Applicant is reminded that when the claim is directed to a product, the preamble is generally nonlimiting if the body of the claim is directed to an old composition and the preamble merely recites a property inherent in the old composition. [*Kropa v. Robie*, 88 USPQ 478, 480 - 81 (CCPA 1951); see also MPEP 2111.02.

Applicant is reminded that the intended use of a product claim carries no patentable weight [MPEP 2111.02].

The method in which the primers were produced is immaterial to their patentability. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

Claim Rejections - 35 U.S.C. § 103

19. Claims 2, 8, 9, and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Accession AC005277, IDS AN.

AC005277 is a polynucleotide of at least 15 nucleotides which hybridizes to the nucleic acid of claim 1, and has a nucleotide sequence encompassed by claim 8. Although AC005277 fails to teach a primer pair, use of primer pair would be an obvious variation of the invention. Primers are well known to be useful for detection and research and a primer pair is known to provide confirmatory and correlating data.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Hunt, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Hunt

February 25, 2001